mented with regional cerebral perfusion may provide better cerebral protection than more conventional techniques.

Although the data presented by Pigula, Siewers, and Nemoto are suggestive of adequate cerebral protection, we still believe that core cooling to 18°C is the principal component of our cerebral protection strategy. Further study is warranted to ascertain the relative merits of regional cerebral perfusion versus hypothermia for cerebral protection during aortic arch reconstruction in the neonate.

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Drug therapy before coronary artery operations

To the Editor:

We were greatly interested by the results of the IMAGE trial,[1] which suggests European patients are more susceptible than US patients to aprotinin-induced vein graft occlusion. This has prompted us to inquire whether our patients have a European or US response to aprotinin.

We have used aprotinin in varying doses for patients undergoing redo operations or for those with recent aspirin ingestion. Table I describes our mortality rate in consecutive patients undergoing coronary artery bypass grafting with or without other procedures between 1993 and 1998; a dose-dependent increase in mortality is evident. However, the indications for aprotinin are also very important risk factors for perioperative mortality. Thus it may not be too surprising that patients given aprotinin have a higher mortality rate. To clarify this, we have further analyzed our data to take risk factors for mortality into account.

The patients and model have been described in detail elsewhere.[2] Logistic regression was performed with in-hospital mortality from any cause as the dependent factor and 22 independent factors: age, sex, urgency of the operation, history of cardiac surgery, concurrent cardiac or cardiovascular procedures, left ventricular function, recent myocardial infarct, left main coronary artery stenosis, chronic airways disease, cerebrovascular disease, diabetes, hypertension, and other risk factors including preoperative cardioactive drug use. Stepwise regression was not used.

In this model we found the relative risk of mortality attributable to aprotinin to be 1.34 per million units of aprotinin with 95% confidence intervals of 1.1 to 1.7 (P = .01 for relative risk = 1). This indicates a risk-adjusted association between aprotinin and in-hospital mortality.

In the jargon of evidence-based medicine, our data are

Table I. *Dose of aprotinin, number of patients, and in-hospital mortality rate for 1593 consecutive patients undergoing coronary artery operations*

Dose of aprotinin (10^6 KIU)	*n*	*Mortality rate (%)*
0	839	1.8
<1	248	3.2
1-1.9	191	3.1
2-2.9	201	6.5
3-3.9	62	9.7
≥4	52	11.5

"class III evidence" and should not be considered conclusive. However, taken in conjunction with the IMAGE trial results, our data support the hypothesis that in some circumstances aprotinin may have a deleterious effect on patients undergoing coronary artery operations.

We do not understand why aprotinin appears to have adverse effects in some surgical units and not others. We use balanced salt solutions for vein distention, maintain kaolin-activated clotting times above 600 seconds, and never administer our blood cardioplegic solution through vein grafts. Until it becomes clear why the adverse effects of aprotinin appear to be site specific, we would suggest that aprotinin should be used with caution in coronary artery operations.

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Reply to the Editor:

The letter by Weightman and Newman suggests a dose-dependant mortality for aprotinin doses ranging from 0 to ≥4,000,000 KIU (see their Table I). In the IMAGE study (J Thorac Cardiovasc Surg 1998;116:716-30), the average dose in aprotinin-treated patients was 5,550,000 KIU (n = 436). This total includes the 2,000,000 KIU loading dose, 2,000,000 KIU into the cardiopulmonary bypass circuit prime, plus 1,570,000 KIU by continuous infusion at a prescribed rate of 500,000 KIU per hour. IMAGE study results showed that this administration regimen for aprotinin had no effect on mortality (placebo, 1.6%; aprotinin, 1.4%). In the